# Crossing borders in minimally invasive pancreatic and liver surgery

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# CHAPTER 4

## Multicentre analysis of robotic versus laparoscopic distal pancreatectomy

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# ABSTRACT

**Background:** The role of minimally invasive distal pancreatectomy is still unclear, and whether robotic distal pancreatectomy (RDP) offers benefits over laparoscopic distal pancreatectomy (LDP) is unknown because large multicenter studies are lacking. This study compared perioperative outcomes between RDP and LDP.

**Methods:** A multicenter international propensity score-matched study included patients who underwent RDP or LDP for any indication in 21 European centers from six countries that performed at least 15 distal pancreatectomies annually (January 2011 to June 2019). Propensity score-matching was based on preoperative characteristics in a 1:1 ratio. The primary outcome was the major morbidity rate (Clavien-Dindo grade IIIa or above).

**Results:** A total of 1551 patients (407 RDP and 1144 LDP) were included in the study. Some 402 patients who had RDP were matched with 402 who underwent LDP. After matching, there was no difference between RDP and LDP groups in rates of major morbidity (14.2 versus 16.5% respectively, $p$=0.378), postoperative pancreatic fistula grade B/C (24.6 versus 26.5%, $p$=0.543), or 90-day mortality (0.5 versus 1.3%, $p$=0.268) did not differ between RDP and LDP, respectively. RDP was associated with a longer duration of surgery than LDP (median 285 minutes [interquartile range {IQR} 225-350] versus 240 [195-300] min respectively, p<0.001), lower conversion rate (6.7 versus 15.2%, $p$<0.001), higher spleen preservation rate (81.4% versus 62.9%, $p$=0.001), longer hospital stay (median 8.5 [IQR 7-12] versus 7 [IQR 6-10] days, p<0.001) and lower readmission rate (11.0% versus 18.2%, $p$=0.004).

**Conclusion:** The major morbidity rate was comparable between RDP and LDP. RDP was associated with improved rates of conversion, spleen preservation and readmission to the detriment of longer duration of surgery and hospital stay.

# INTRODUCTION

Minimally invasive distal pancreatectomy (MIDP) is being used increasingly for benign and low-grade malignant tumors, as supported by the 2019 Miami evidence based guidelines.[1] Two randomized controlled trials, LEOPARD and LAPOP, demonstrated less blood loss, less delayed gastric emptying and shorter time to functional recovery for the minimally invasive approach without obvious downsides, compared with the open approach.[2,3] These findings confirmed those of previous cohort studies and systemic reviews.[4–7] Yet, the high rate of conversion to open distal pancreatectomy and lack of clear evidence concerning the oncological outcomes of MIDP hamper further implementation.[4,8]

Although MIDP has been implemented over the past decade,[9,10] consensus regarding the benefit of the robotic compared with the laparoscopic approach is lacking.[11–13] Several meta-analyses and a propensity score-matched study have suggested comparable surgical outcomes between the two approaches in terms of overall morbidity[14–16] and the rate of postoperative pancreatic fistula .[14,17] However, studies are limited by their retrospective, mainly single-center design with a clear risk of selection bias.[15] A multicenter international comparison in experienced pancreatic centers practicing one or both modalities is currently lacking.

The present study aimed to compare surgical outcomes of robotic (RDP) and laparoscopic (LDP) distal pancreatectomy for all indications performed in experienced centers using propensity score-matching. The primary hypothesis was that the rate of major morbidity would not differ between RDP and LDP.

# METHODS

This study was conducted according to the STROBE guidelines.[18] The medical ethics review committee of the Amsterdam UMC, location Amsterdam Medical Center, waived the need for informed consent owing to the retrospective observational study design. All centers participating in the European consortium on Minimally Invasive Pancreatic Surgery (E-MIPS) were invited to contribute. Participating centers had to perform at least 15 distal pancreatectomies annually. Consecutive patients, aged 18 or higher, who underwent RDP or LDP for benign and malignant diseases between January 2011 and June 2019 were included. All participating centers received a database with the required parameters including definitions. Data were then collected locally using prospective collected databases and combined centrally by the study coordinators.

## Definitions

Conversion was defined as any resection started as minimally invasive procedure (laparoscopic or robotic) which required laparotomy or hand assistance for other reasons than trocar placement or specimen extraction.[19] Intended spleen preservation was noted when spleen preserving distal pancreatectomy was the aim of the surgery at the surgeons or multidisciplinary team discretion, based on preoperative imaging. Some tumors, such as intraductal papillary mucinous neoplasms and solid pseudopapillary neoplasm could have invasive characteristics and were categorized as premalignant. Neuroendocrine tumors were categorized according to the WHO 2010 classification for neuroendocrine neoplasms of the digestive system.[20]

Postoperative morbidity was scored and classified according to the Clavien-Dindo classification of surgical complications and recorded up to 30 days postoperatively.[21] The primary outcome of this study was major morbidity defined as Clavien-Dindo grade IIIa or higher. For pancreas-specific complications (postoperative pancreatic fistula, delayed gastric emptying and post pancreatectomy hemorrhage) only grade B/C complications were noted, following the most recent definitions of the International Study Group on Pancreatic Surgery (ISGPS).[22–24] Readmissions and deaths were recorded up to 90 days after surgery.

## Statistical analysis

Statistical analysis was performed using IBM SPSS® Statistics for Windows version 26.0 (IBM, Armonk, NY, USA). The two independent Student's t-test was used for comparison of normally distributed continuous variables, which are reported as mean (SD) values. Non-normally distributed variables are presented as median (IQR) values, and compared using the Mann-Whitney U test. Normality of continuous variables was checked visually using histograms. Categorical variables were reported as counts with proportions and analyzed with the Chi square or Fisher's exact test, as appropriate.

To minimize the impact of selection bias, patients undergoing RDP and LDP were matched using propensity scoring. Propensity scores were based on variables known from literature associated with treatment assignment and included the baseline variables age (continuous), sex, ASA physical status, intention of spleen preservation and type of tumor (benign, (pre)malignant, pancreatic ductal adenocarcinoma (PDAC) or other type [i.e. chronic pancreatitis]). Matching without replacement was done with a 1:1 ratio, based on nearest neighbors and with a caliper width of 0.01 standard deviation. Standardized mean differences (MDs) were calculated for the assessment of distribution of baseline co-variables between the two groups.[25] The MD was calculated only for baseline characteristics. A MD on or between -0.1 and 0.1 was considered the optimal balance. After matching, normally distributed continuous data were compared using the paired samples t-test. For non-normally distributed continuous data, the Wilcoxon signed rank test was used. Categorical data were compared using McNemar's test. Additionally, to test whether potential confounders for the primary outcome were not corrected for in the propensity score matching, a multivariable binary logistic regression analysis with backward selection was performed on the unmatched cohort with previously described risk factors associated with major morbidity. The results are reported as odds ratios (ORs) with 95% confidence intervals.

To investigate the selection criteria for RDP, both univariable and multivariable binary logistic regression analyses with backward selection were performed for baseline characteristics in the total cohort. Variables included in the analysis were based on the assumption that RDP, a more novel technique, was performed for younger patients, with a lower ASA grade and more often for non-malignant tumors. Because RDP has shown to preserve the spleen more often in small studies, this was considered as well.



Two sensitivity analyses were performed. First, hospitals that performed fewer than 15 RDP or LDP procedures per year on average in 2017 and 2018 were excluded. These two complete years were chosen because the annual number of MIDPs increased during the study period in all participating centers and there were only 6 months in 2019. Second, patients operated on in one of the two countries with the longest hospital stay were excluded to investigate the impact on hospital stay of differences in healthcare systems. The level of statistical significance was set at a two-sided *p*-value <0.050.

# RESULTS

Of 1551 MIDPs, 407 (26.2%) were RDP and 1144 (73.8%) were LDP procedures (*Table* 1). RDP was performed in and LDP in 19 of the 21 centers. Use of RDP increased from 22.7% (80 of 353) in 2011-2013 to 32.2% (185 of 390) in 2017-2019 (p< 0.001) (Fig. S1). Overall, 59.4% of patients were women (n= 921), mean (SD) age was 59 (± 26) years, and mean (SD) BMI 25.7 (4.9) kg/m$^2$. In 406 out of 563 patients (69.5%) with intended spleen preservation, the spleen was successfully-preservation. Patients undergoing RDP were younger than those who had LDP (mean (SD) age 57 (15) vs 60 (15) years respectively, MD 0.20). Patients undergoing RDP had a lower rate of PDAC (16.0 vs 21.1% in the LDP group; MD 0.18) and a higher intended spleen preservation rate (47.3 vs 33.5% respectively, SMD -0.32) (Table 1).

## Potential confounders for primary outcome

In multivariable logistic regression analysis performed to identify potential variables associated with major morbidity, only ASA grade (III/IV) and multivisceral resection

**Table 1. Baseline characteristics for robotic and laparoscopic distal pancreatectomy before and after propensity score matching**

| | Total cohort | | | | Propensity score-matched cohort | | | |
|---|---|---|---|---|---|---|---|---|
| | **Robotic (n=407)** | **Laparoscopic (n=1 144)** | ***P*-value** | **SMD** | **Robotic (n=402)** | **Laparoscopic (n=402)** | ***P*-value** | **SMD** |
| Age, years, mean (SD) | 57 (14.5) | 60 (15.1) | 0.002 | 0.20 | 57 (14.8) | 57 (14.2) | 0.673 | 0.00 |
| Age ≥ 65, years, n, (%) | 145 (35.6) | 494 (43.2) | 0.008 | 0.18 | 144 (35.8) | 154 (38.3) | 0.465 | 0.06 |
| Female sex, n (%) | 240 (59.0) | 681 (59.6) | 0.829 | 0.01 | 237 (59.0) | 244 (60.7) | 0.615 | 0.04 |
| BMI, kg/m$^2$, mean (SD) | 25.4 (4.5) | 25.9 (5.0) | 0.099 | 0.10 | 25.4 (4.6) | 25.9 (5.0) | 0.215 | 0.10 |
| ≥ 30.0 | 67 (17.7) | 186 (19.0) | 0.595 | 0.05 | 67 (17.9) | 66 (18.9) | 0.743 | 0.03 |
| Unknown | 29 | 164 | | | 28 | 52 | | |
| ASA classification III-IV, n (%) | 93 (22.9) | 278 (25.8) | 0.257 | 0.09 | 92 (22.9) | 87(21.6) | 0.672 | -0.04 |
| Unknown | 7 | 65 | | | 0 | 5 | | |
| Prior abdominal surgery, n (%) | 167 (41.0) | 478 (42.9) | 0.504 | 0.04 | 165 (41.0) | 152 (38.3) | 0.426 | -0.06 |
| Unknown | 20 | 50 | | | 0 | 0 | | |
| Tumour size preoperative, mm, mean (SD) | 33 (20.3) | 32 (20.0) | 0.642 | -0.05 | 33 (20.3) | 32 (19.2) | 0.399 | -0.05 |
| Size >50mm, n (%) | 58 (18.3) | 156 (16.0) | 0.328 | -0.09 | 58 (18.5) | 59 (16.6) | 0.529 | -0.07 |
| Unknown | 90 | 166 | | | 88 | 47 | | |
| Tumour type, n (%) | | | 0.102 | 0.08 | | | 0.180 | -0.10 |
| Benign | 210 (51.7) | 539 (47.2) | | | 206 (51.2) | 212 (52.7) | | |
| (Pre)malignant | 111 (27.3) | 318 (27.9) | | | 111 (27.6) | 121 (30.1) | | |
| PDAC | 65 (16.0) | 241 (21.1) | 0.027 | 0.18 | 65 (16.2) | 60 (14.9) | 0.558 | -0.06 |
| Other (including chronic pancreatitis) | 20 (4.9) | 43 (3.8) | | | 20 (5.0) | 9 (2.2) | | |
| Unknown | 1 | 3 | | | 0 | 0 | | |
| Intended spleen preservation, n (%) | 192 (47.3) | 371 (33.5) | <0.001 | -0.32 | 188 (46.8) | 190 (47.3) | 0.888 | 0.01 |
| Unknown | 1 | 38 | | | 0 | 0 | | |

*BMI* indicates body mass index, *ASA* American Society of Anaesthesiologists, *SMD* standardised mean difference, *PDAC* pancreatic ductal adenocarcinoma. SMD calculated for both the total and propensity score matching cohort. SMD on or between -0.1 and 0.1 was considered optimal variable balance. Premalignant inclused invasive intraductal papillary mucinous neoplasms and mucinous cystic neoplasm.

were significant (OR 1.66 [95% CI 1.12 to 2.46], $p$= 0.011 and OR 3.65 [2.04 to 6.53], $p$<0.001, respectively)(Table S1).

### Selection criteria for robotic distal pancreatectomy

Potential selection criteria for RDP were analyzed using univariable analysis in the entire cohort of 1551 patients, including age (less than 65 versus 65 years or more), sex (male versus female), BMI (continuous), ASA grade (I-II versus III-IV), previous abdominal surgery (yes versus no), intended spleen preservation (yes versus no), tumor size (50 mm or less versus more than 50 mm), and tumor type (benign, (pre)malignant, PDAC or other). In multivariable analysis, only ASA grade I-II (OR 1.47 [95% CI 1.06-2.05], $p$= 0.022) and intended spleen preservation (OR 1.74 [1.33-2.29], $p$< 0.001) were associated with the use of RDP (Table S2).



### Matched cohort

Of the 407 patients who underwent RDP, 402 patients (98.8%) could be matched with 402 patients who had LDP. After matching, baseline characteristics were well balanced, indicated by MD values below 0.1 (Table 1). There were no statistically significant differences between the matched RDP and LDP groups for the proportion of resected PDAC (16.2 versus 14.9% respectively; MD -0.06), or for mean (SD) pathological tumor size (31 [SD 19] versus 32 [SD 21] mm, $p$= 0.240)(Table 2). RDP was associated with a greater number of resected lymph nodes than LDP (median 14 [IQR 7-24] versus 10 [3-18], $p$= 0.003), yet the number of metastatic lymph nodes was similar.

RDP was associated with a higher rate of spleen preservation than LDP (81.4% vs 62.4% respectively, p= 0.001). The Kimura technique[26] (splenic vessel preservation) for spleen preservation was used more often in the RDP group (92.6 vs 73.2% in the LDP group, p< 0.001) (Table 3). In addition, RDP was associated with a lower conversion rate (6.7 versus 15.2% respectively, p< 0.001) and a longer duration of surgery (median 285 [IQR 225-350] versus 240 [195-300] min, p< 0.001).

Major morbidity was comparable between RDP and LDP: 14.2 versus 16.5% respectively ($p$= 0.378). In addition, rates of postoperative pancreatic fistula grade B/C in RDP and LDP groups (24.6 versus 26.5% respectively, $p$= 0.543), reoperation (5.2 versus 5.5%, $p$= 0.875) and 90-day mortality (0.5 versus 1.3%, $p$= 0.268) were not significantly different. RDP was associated with a longer hospital stay than LDP (median 8.5 [IQR 7-12] versus 7 [6-10] days, $p$< 0.001) and a lower readmission rate (11.0% versus 18.2%, $p$= 0.004).

### Sensitivity analysis

After excluding the procedures performed in hospitals with an average annual volume of fewer than 15 MIDP procedures in 2017 and 2018, the major morbidity rate remained

**Table 2. Pathology before and afterpropensity score-matching**

| | Total | | | Propensity score-matched | | |
|---|---|---|---|---|---|---|
| | **Robotic (n=407)** | **Laparoscopic (n=1 144) )** | ***P*-value** | **Robotic (n=402)** | **Laparoscopic (n=402)** | ***P*-value** |
| Tumour type, n (%) | | | 0.011 | | | 0.098 |
| Neuroendocrine tumour* | 131 (32.3) | 331 (29.0) | | 129 (32.1) | 124 (30.8) | |
| G1/G2 | 123 (98.4) | 293 (98.3) | | 121 (98.4) | 108 (98.2) | |
| G3 | 2 (1.6) | 5 (1.7) | | 2 (1.6) | 2 (1.8) | |
| Unknown | 6 | 33 | | 6 | 14 | |
| Pancreatic ductal adenocarcinoma | 65 (16.0) | 241 (21.1) | | 65 (16.2) | 60 (14.9) | |
| Mucinous cystic neoplasm | 61 (15.0) | 142 (12.4) | | 60 (14.9) | 44 (10.9) | |
| Serous cystadenoma | 42 (10.3) | 87 (7.6) | | 42 (10.4) | 36 (9.0) | |
| Intraductal papillary mucinous neoplasms | 40 (9.9) | 144 (12.6) | | 40 (10.0) | 53 (13.2) | |
| Solid pseudopapillary tumour | 23 (5.7) | 44 (3.9) | | 22 (5.5) | 24 (6.0) | |
| Chronic pancreatitis/pseudocyst | 13 (3.2) | 43 (3.8) | | 13 (3.2) | 17 (4.2) | |
| Metastases (including RCC) | 4 (1.0) | 37 (3.2) | | 4 (1.0) | 12 (3.0) | |
| Other cystic lesion | 7 (1.7) | 24 (2.1) | | 7 (1.7) | 14 (3.5) | |
| Other malignant tumour | 2 (0.5) | 14 (1.2) | | 2 (0.5) | 7 (1.7) | |
| Other | 18 (4.4) | 35 (3.1) | | 18 (4.5) | 11 (2.8) | |
| Unknown | 1 | 2 | | 0 | 0 | |
| Tumour size, mm, mean (SD) | 30 (18.7) | 33 (21.4) | 0.035 | 31 (18.8) | 32 (21.1) | 0.240 |
| Lymph nodes resected (malignant tumours only), median (IQR) | 14 (6-24) | 12 (5-22) | 0.073 | 14 (7-24) | 10 (3-18) | 0.003 |
| Lymph nodes (tumour positive only), median (IQR) | 0 (0-2) | 0 (0-2) | 0.578 | 0 (0-2) | 0 (0-2) | 0.508 |
| R0 resection for pancreatic ductal adenocarcinoma, n (%)+ | 50 (76.9) | 115 (64.9) | 0.066 | 40 (69.0) | 51 (78.5) | 0.231 |

*RCC* indicates renal cell carcinoma. *Neuroendocrine tumours include insulinoma and glucagonoma and are classified according to the WHO 2010 definitions.
+R0 is defined as microscopic radical resection of ≥ 1mm between tumour at the transection or retroperitoneal margin.

**Table 3. Operative details and outcomes before and after propensity score-matching**

| | Total | | | Propensity score-matched | | |
|---|---|---|---|---|---|---|
| **Operative details** | **Robotic (n=407)** | **Laparoscopic (n=1 144)** | ***P*-value** | **Robotic (n=402)** | **Laparoscopic (n=402)** | ***P*-value** |
| Operative time, min, median (IQR) | 285 (225-350) | 240 (191-300) | <0.001 | 285 (225-350) | 240 (195-300) | <0.001 |
| Blood loss, ml, median (IQR) | 150 (100-250) | 120 (70-250) | 0.956 | 150 (100-250) | 150 (80-250) | 0.717 |
| Unknown | 90 | 304 | | 86 | 99 | |
| Blood transfusion, n (%) | 16 (4.5) | 34 (3.5) | 0.424 | 16 (4.6) | 9 (2.7) | 0.196 |
| Unknown | 51 | 185 | | 51 | 69 | |
| Conversion, n (%) | 27 (6.6) | 174 (15.2 | <0.001 | 27 (6.7) | 61 (15.2) | <0.001 |
| Stump closure method, n (%) | | | <0.001 | | | <0.001 |
| Stapler | 147 (42.0) | 823 (75.4) | | 146 (42.2) | 311 (79.3) | |
| Sutures | 115 (32.9) | 145 (13.3) | | 115 (33.2) | 35 (8.9) | |
| Ultrasonic device | 85 (24.3) | 110 (10.1) | | 82 (23.7) | 42 (10.7) | |
| Other | 3 (0.9) | 14 (1.2) | | 3 (0.9) | 4 (1.0) | |
| Unknown | 57 | 52 | | 56 | 10 | |
| Splenectomy, n (%) | 246 (60.6) | 863 (75.5) | <0.001 | 246 (61.2) | 276 (68.7) | 0.027 |
| Spleen preservation intended and actually preserved, n (%)* | 157 (80.5) | 249 (64.0) | <0.001 | 153 (80.1) | 122 (62.9) | 0.001 |
| Method of spleen preservation | | | <0.001 | | | <0.001 |
| Splenic-vessel preservation (Kimura+) | 114 (92.7) | 173 (73.6) | | 112 (92.6) | 82 (73.2) | |
| Splenic-vessel resection (Warshaw~) | 9 (7.3) | 62 (26.4) | | 9 (7.4) | 30 (26.8) | |
| Unknown | 38 | 37 | | 35 | 11 | |
| Multi-visceral resection, n (%) | 13 (3.8) | 76 (7.0) | 0.036 | 13 (3.9) | 24 (6.2) | 0.153 |
| Unknown | 68 | 56 | | 66 | 16 | |
| Vascular resection, n (%) | 10 (2.9) | 12 (1.2) | 0.023 | 10 (3.0) | 4 (1.1) | 0.077 |

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| | Total | | | Propensity score-matched | | |
|---|---|---|---|---|---|---|
| **Operative details** | **Robotic (n=407)** | **Laparoscopic (n=1 144)** | ***P*-value** | **Robotic (n=402)** | **Laparoscopic (n=402)** | ***P*-value** |
| PV/SMV | 2 (0.6) | 8 (0.8) | | 2 (0.6) | 2 (0.6) | 0.125 |
| Other such as renal vein | 8 (2.3) | 4 (0.4) | | 8 (2.4) | 2 (0.6) | |
| Unknown | 68 | 112 | | 66 | 39 | |
| **Postoperative outcomes** | | | | | | |
| Major morbidity (Clavien-Dindo ≥3a), n (%) | 57 (14.1) | 175 (15.4) | 0.516 | 57 (14.2) | 66 (16.5) | 0.378 |
| Postoperative transfusion, n (%) | 24 (7.0) | 101 (9.4) | 0.178 | 24 (7.1) | 32 (8.3) | 0.536 |
| Drain removed, days, median (IQR) | 7 (4-15) | 6 (4-14) | 0.095 | 7 (4-15) | 6 (4-13) | 0.037 |
| Postoperative pancreatic fistula, grade B/C, n (%) | 99 (24.3) | 258 (22.6) | 0.481 | 99 (24.6) | 106 (26.5) | 0.543 |
| Intervention for POPF, n (%) | 35 (8.6) | 117 (10.3) | 0.336 | 35 (8.7) | 49 (12.3) | 0.101 |
| Delayed gastric emptying grade B/C, n (%) | 11 (3.0) | 16 (1.5) | 0.069 | 11 (3.0) | 7 (1.8) | 0.282 |
| Postpancreatectomy haemorrhage grade B/C, n (%) | 16 (4.2) | 51 (4.7) | 0.665 | 16 (4.2) | 20 (5.1) | 0.541 |
| Reoperation, n (%) | 21 (5.2) | 61 (5.3) | 0.899 | 21 (5.2) | 22 (5.5) | 0.875 |
| Hospital stay, days, median (IQR) | 8 (7-12) | 7 (6-10) | <0.001 | 8.5 (7-12) | 7 (6-10) | <0.001 |
| Readmission, n (%) | 44 (10.8) | 181 (16.0) | 0.011 | 44 (11.0) | 73 (18.2) | 0.004 |
| 90-day mortality, n (%) | 2 (0.5) | 10 (0.9) | 0.462 | 2 (0.5) | 5 (1.3) | 0.268 |

*PV/SMV* indicates portal vein or superior mesenteric vein POPF postoperative pancreatic fistula.
*proportion of actual spleen preservation when intended preoperately.
[+]Kimura W, et al. Spleen preserving distal pancreatectomy with conservation of the splenic artery and vein. Surgery. 1996; 120: 885–890. ~Warshaw AL. Conservation of the Spleen With Distal Pancreatectomy. Arch Surg. 1988; 123: 550–553.

comparable in RDP and LDP groups (14.9 versus 15.8% respectively, $p= 0.745$) (Table S3). Other short-term surgical outcomes were also similar to those in the main analysis. The conversion rate was 5.9 versus 14.8% respectively, $p< 0.001$.

After excluding all RDP and LDP procedures from the two countries with the longest hospital stay (Germany and France) from the matched cohort, the median duration of hospital stay was 8 (IQR 6-11) versus 7 (6-10) days, for RDP and LDP respectively P<0.001. (Table S4). RDP was associated with a lower readmission rate (11.6 versus 18.8% in the LDP group, $p= 0.009$).

## DISCUSSION



This multicenter study including over 1500 MIDPs from 21 European centers found that after propensity score-matching, there was no difference between RDP and LDP in the rate of major morbidity. In addition, the rates of postoperative pancreatic fistula grade B/C and 90-day mortality did not differ significantly between the two procedures. RDP was associated with improved rates of spleen preservation, conversion, and readmission to the detriment of a longer duration of surgery and longer hospital stay.

Use of the robotic approach for abdominal surgery is increasing worldwide.[27] Although some RCTs have indicated superiority or at least non-inferiority, for robotic compared with open surgery [28] [29], additional advantages over a laparoscopic approach have not been well established.[30–32] The first RDP procedure was reported in 2003.[33] Although retrospective single-center studies[11,13,16] and a national study using the National Surgical Quality Improvement Program database[34], suggested a benefit for RDP in terms of spleen preservation and conversion, only 16% of surgeons are performing RDP according to a recent worldwide survey on minimally invasive pancreatic surgery.[35]

The present multicenter international study found an increased use of RDP with time, from 22.7% in 2011-2013 to 32.2% in 2017-2019. Before propensity score matching, RDP was used more often in younger patients, more often with an intention for spleen preservation, but RDP was used less in patients with PDAC. This may be explained by the fact that this study included the very first and subsequent RDP procedures from 11 centers, whereas the 19 centers contributing LDP were mostly already ahead of the learning curve for this approach. Indeed, single-center and nationwide studies on the implementation of LDP have shown that, with increasing experience, surgeons extend their indications for the minimally invasive approach, including older patients and more often PDAC.[9,36]

However, because RDP is often associated with increased spleen preservation rates,[11,37,38] surgeons may have used the robotic approach more often when spleen preservation is preferred for a patient. Intended spleen preservation was indeed a factor associated with RDP. To adjust for baseline differences between the two modalities, groups were matched by means of propensity scoring, after which these differences were mitigated. Following matching, the present study confirmed previous reported advantages of the robotic approach in terms of a reduced conversion rate and increased spleen preservation, even though the PDAC rate was similar in the two groups.[13,16,37,38]

A lower conversion rate is a frequently mentioned advantage of the robotic approach owing to greater dexterity[16] or better visualization[39] with the robot. However the learning curve aspect of MIDP should also be taken in account. With increasing experience, conversion rates during MIDP decrease, with a cut-off point of 15 consecutive MIDPs.[40] Potentially, the surgeons performing RDP had already gained their initial experience in the minimally invasive approach to distal pancreatectomy and therefore required fewer conversions. Interestingly, after excluding centers performing less than 15 MIDPs annually in the first sensitivity analysis, RDP was still associated with a lower conversion rate, indicating an inherent advantage of the robotic platform.

With improved understanding of the potential sequelae of splenectomy, including the risk of hospitalization and/or mortality from infectious disease, venous thromboembolism and solid or hematological malignancy[41], spleen preservation is advocated increasingly during distal pancreatectomy.[42,43] In the present study, spleen preservation was intended for over one-third of patients and succeeded in 72.1% of these procedures. After matching, RDP was associated with a higher spleen preservation rate than was seen during LDP. In addition, splenic vessel preservation (Kimura technique[26]) was used more often in RDP than in LDP, whereas splenic vessel resection (Warshaw technique[44]) was more often applied in LDP. The Warshaw technique is used mainly when the Kimura technique is not feasible due to tumor involving the splenic vessels, intraoperative technical difficulty in preserving the splenic vessels, or persistent blood loss from splenic vessels.[37,45,46] Splenic vessel preservation requires meticulous dissection of the splenic vessels from the pancreas and control of small perforating blood vessels in order to prevent bleeding. The robotic system may facilitate this dissection owing to the articulating instruments and improved control over excessive bleeding.[16,38]

Randomized studies comparing RDP with LDP are lacking. Although both modalities were included in the Dutch LEOPARD trial, only 5 of 47 minimally invasive procedures in that study were performed using the robotic approach.[2] The LAPOP trial included only LDP.[3] Several other trials are comparing minimally invasive with open distal pancreatectomy (NCT03957135 and NCT03792932). Nevertheless, these trials include only LDP. For pancreatic cancer, the ongoing DIPLOMA trial in patients with pancreatic cancer (ISRCTN44897265) includes both LDP and RDP.

The study has limitations. The inherent drawback of retrospective studies is treatment allocation bias. Although both groups were well balanced after propensity score matching, treatment groups may still differ in unmeasured and unmatched risk factors. For example, details regarding the specific location of the tumor in the pancreatic body or tail or the tumor proximity to the splenic vessels were missing, and this may have influenced the differences in rate of successful spleen preservation. Yet, tumor size of 30 mm or more has been described as the only risk factor for unplanned splenectomy during LDP.[42]

The validity of the data on intended spleen preservation can be criticized given the retrospective design of the study, although they were collected from prospective institutional collected databases. Additionally, all patients were counselled before surgery regarding the extension of the operation including resection of the spleen and this was registered in patients' files.

RDP is an expensive surgical technique. Unfortunately, a cost or quality-adjusted life-year analysis was not feasible to perform owing to cross-border differences in healthcare systems and missing data, including consumables, imaging, and duration of readmission. Single-center studies from Europe and the USA have reported similar cost-effectiveness for RDP in comparison with LDP, whereas other studies have shown higher costs for RDP.[47–49]

Differences in healthcare systems may have influenced some of the postoperative outcomes such as hospital stay and readmission rate. In the sensitivity analysis, hospital stay remained significantly longer for RDP than for LDP. A clear explanation for these findings could not be identified as patient characteristics and complication rates were comparable between the two groups. It is possible that the longer hospital stay after RDP prevented some readmissions. Finally, because these data were not available, surgeons' experience and learning curve associated with short-term outcome were not included in the analyses, although this might have influenced the results. Yet, the impact was considered to be minimal due to the multicenter setting, large number of patients, and inclusion of only experienced centers.

Strengths of this study include the multicenter, international setting and the large number of procedures, reflecting the state of RDP in experienced European centers. A multicenter international RCT should confirm the findings while stratifying for intended spleen preservation, and with special emphasis on cost-effectiveness.

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**Supplemental Table 1. Multivariable analysis of parameters associated with major morbidity (n=1 551)**

| | **Multivariable analysis** | |
|---|---|---|
| **Factors** | OR (95% CI) | P-value |
| Age ≥ 65 years (vs. <65) | Removed step 9 | |
| Female sex (vs. male) | Removed step 11 | |
| BMI (continuous) | Removed step 3 | |
| ASA classification III/IV (vs. I-II) | 1.662 (1.121-2.463) | 0.011 |
| Prior abdominal surgery (Yes vs. No) | Removed step 5 | |
| Tumour size >50mm on preoperative imaging (vs. ≤ 50mm) | Removed step 4 | |
| Laparoscopic vs. robotic | Removed step 6 | |
| Multivisceral resection (Yes vs. No) | 3.646 (2.036 – 6.528) | <0.001 |
| Vascular resection (Yes vs. No) | Removed step 8 | |
| Splenectomy (Yes vs. No) | Removed step 2 | |
| Conversion to open (Yes vs. No) | Removed step 7 | |
| Tumour type | Removed step 10 | |
| Benign | Ref | |
| (Pre)malignant | | |
| PDAC | | |
| Other | | |
| Year of surgery | Removed step 12 | |
| 2011-2013 | Ref | |
| 2014-2016 | | |
| 2017-2019 | | |

*OR* odds ratio, *BMI* Body mass index, *CI* Confidence interval, *ASA* American Society of Anaesthesiologists. *PDAC* pancreatic ductal adenocarcinoma

**Supplemental Table 2. Univariable and multivariable analysis of baseline characteristics to define selection criteria for the robotic approach (n=1 551)**

| | **Univariable analysis** | | **Multivariable analysis** | |
|---|---|---|---|---|
| **Factors** | OR (95% CI) | *P*-value | OR (95% CI) | *P*-value |
| Age ≥ 65 years (vs. <65) | 0.727 (0.575-0.919) | 0.008 | Removed step 6 | |
| Female sex (vs. male) | 1.026 (0.815 -1.291) | 0.829 | Removed step 2 | |
| BMI (continuous) | 0.979 (0.955-1.004) | 0.099 | Removed step 7 | |
| ASA classification I-II (vs. III/IV) | 0.856 (0.654-1.120) | 0.257 | 1.472 (1.057-2.050) | 0.022 |
| Prior abdominal surgery (Yes vs. no) | 0.924 (0.734-1.164) | 0.504 | Removed step 3 | |
| Tumour size >50mm (vs. ≤ 50mm)* | 1.180 (0.846-1.645) | 0.329 | Removed step 4 | |
| Tumour type | | | Removed step 5 | |
| Benign | Ref | | | |
| (Pre)malignant | 0.896 (0.685-1.172) | 0.422 | | |
| PDAC | 0.692 (0.504-0.950) | 0.023 | | |
| Other | 1.194 (0.686-2.077) | 0.531 | | |
| Intended spleen preservation (Yes vs. no) | 1.777 (1.410-2.240) | <0.001 | 1.744 (1.331-2.286) | <0.001 |

*OR* odds ratio, *BMI* Body mass index, *CI* Confidence interval, *ASA* American Society of Anaesthesiologists, PDAC Pancreatic ductal adenocarcinoma
* on preoperative imaging

Chapter 4

**Supplemental Table 3. Sensitivity analysis of outcomes including centres (n= 11) performing a mean of ≥ 15 MIDPs in 2017 and 2018.**

| | Robotic (n=324) | Laparoscopic (n=291) | *P*-value |
|---|---|---|---|
| **Operative details** | | | |
| Operative time, min, median (IQR) | 285 (230-350) | 240 (194-300) | <0.001 |
| Blood loss, ml, median (IQR) | 150 (100-300) | 150 (100-300) | 0.141 |
| Conversion, n (%) | 19 (5.9) | 43 (14.8) | <0.001 |
| Spleen preservation intended and actually preserved, n (%) | 116 (77.3) | 80 (58.8) | <0.001 |
| **Pathology** | | | |
| Tumour type, n (%) | | | 0.122 |
| Benign | 174 (53.7) | 151 (51.9) | |
| (Pre)malignant | 78 (24.1) | 88 (30.2) | |
| Pancreatic ductal adenocarcinoma | 53 (16.4) | 44 (15.1) | |
| Other | 19 (5.9) | 8 (2.7) | |
| **Postoperative outcomes** | | | |
| Major morbidity (Clavien-Dindo ≥3a), n (%) | 48 (14.9) | 46 (15.8) | 0.745 |
| Postoperative pancreatic fistula, grade B/C, n (%) | 87 (26.9) | 83 (28.7) | 0.606 |
| Intervention for POPF, n (%) | 31 (9.6) | 37 (12.8) | 0.203 |
| Delayed gastric emptying grade B/C, n (%) | 11 (3.7) | 6 (2.1) | 0.274 |
| Postpancreatectomy haemorrhage grade B/C, n (%) | 16 (5.2) | 16 (5.7) | 0.795 |
| Reoperation, n (%) | 21 (6.5) | 14 (4.8) | 0.372 |
| Hospital stay, days, median (IQR) | 9 (7-12) | 7 (5-9) | <0.001 |
| Readmission, n (%) | 40 (12.3) | 57 (19.7) | 0.013 |
| 90-day mortality, n (%) | 2 (0.6) | 5 (1.7) | 0.197 |

*POPF* indicates postoperative pancreatic fistula.

**Supplemental Table 4. Sensitivity analysis of outcomes (patients from France and Germany excluded)**

| | Robotic (n=329) | Laparoscopic (n=368) | *P*-value |
|---|---|---|---|
| **Operative details** | | | |
| Operative time, min, median (IQR) | 295 (235-356) | 240 (195-300) | <0.001 |
| Blood loss, ml, median (IQR) | 100 (90-200) | 150 (80-250) | 0.054 |
| Conversion, n (%) | 17 (5.2) | 57 (15.5) | <0.001 |
| Spleen preservation intended and actually preserved, n (%) | 118 (77.1) | 113 (63.5) | 0.007 |
| **Pathology** | | | |
| Tumour type, n (%) | | | 0.077 |
| Benign | 165 (50.2) | 191 (51.9) | |
| (Pre)malignant | 90 (27.4) | 113 (30.7) | |
| Pancreatic ductal adenocarcinoma | 55 (16.7) | 56 (15.2) | |
| Other | 19 (5.7) | 8 (2.2) | |
| **Postoperative outcomes** | | | |
| Major morbidity (Clavien-Dindo ≥3a), n (%) | 43 (13.1) | 58 (15.8) | 0.314 |
| Postoperative pancreatic fistula, grade B/C, n (%) | 82 (24.9) | 95 (26.0) | 0.755 |
| Intervention for POPF, n (%) | 25 (7.6) | 42 (11.5) | 0.084 |
| Delayed gastric emptying grade B/C, n (%) | 3 (1.0) | 7 (2.0) | 0.326 |
| Postpancreatectomy haemorrhage grade B/C, n (%) | 13 (4.2) | 19 (5.3) | 0.503 |
| Reoperation, n (%) | 17 (5.2) | 17 (4.6) | 0.738 |
| Hospital stay, days, median (IQR) | 8 (6-11) | 7 (6-10) | <0.001 |
| Readmission, n (%) | 38 (11.6) | 69 (18.8) | 0.009 |
| 90-day mortality, n (%) | 2 (0.6) | 1 (0.3) | 0.486 |

*POPF* indicates postoperative pancreatic fistula.